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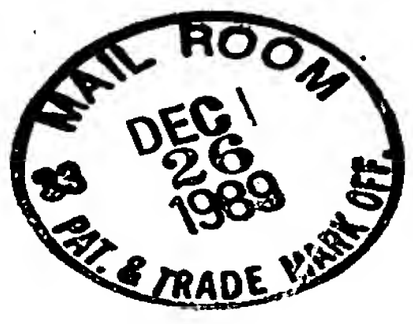

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

3 DAW 1-12-90

In re PATENT Application of

Helmut HETTCHE

Serial No. 07/268,772 Group Art Unit: 158

Filed: November 9, 1988 Examiner: P. Prater

For: AZELASTINE - CONTAINING MEDICAMENTS

December 26, 1989

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Hon. Commissioner of Patents
and Trademarks
Washington, D.C. 20231

Dear Sir:

The applicant respectfully requests reconsideration of the rejection of claims 1-18 in the Office Action dated June 23, 1989.

The basis of the rejection is that the Examiner considers the claimed method, composition and articles to be prima facie obvious from the disclosure of Engel et al patent 4,704,387 in view of four secondary references. Engel et al discloses compounds whose structures are similar to that of the presently claimed azelastine, differing in the R group. In the Engel patent, R is benzyl, phenethyl, methoxyethyl or allyl, whereas, in the present invention, the corresponding group is methyl. Barnes, Ashkenaz, Mendl and Arp are cited in connection with dependent claims 13-17, but are not understood to add to the relevance of Engel et al to applicant's method claims.

While the process of applicant's claims 1-12 may be prima facie obvious, that process is not obvious because it produces an unobvious result. Applicants have conducted comparative experiment which demonstrate this advantage. Regrettably, the results of these experiments have come to

hand only a few days ago, and so there has not been sufficient time to obtain a declaration. Therefore, the data is presented below. We will submit a declaration as soon as it can be obtained, after the Christmas holiday season.

The experiments are based on the fact that an allergic reaction in the eyes or the nose results from the liberation of histamine from mast cells as a result of the action of an antigen. The liberated histamine causes rhinitis symptoms.

The effectiveness of azelastine in preventing these symptoms in the eyes and the nose can be determined by measuring its effectiveness in preventing the liberation of histamine from sensitized rat peritoneal mast cells. The mast cells are incubated first with a test substance and then challenged with antigen. The amount of histamine released is measured, and this is compared with the total potential release of histamine. The amount of inhibition of histamine release is calculated for each test substance.

In the case of azelastine, the inhibition was 47.1% whereas, in the case of the compound of Example 1 of the cited Engel patent, the inhibition was only 24.4%.

Thus, azelastine was about twice as effective as the compound of Example 1 of the Engel patent. This result is surprising and unexpected.

For this reason, it is submitted that the claimed process is unobvious.

In regard to claims 13-17, the Examiner cites In re Durden 763 F.2d 1406 (Fed.Cir. 1985), but that case is not thought to be relevant to the present case. In Durden, the court dealt with the obviousness of a process of making a novel compound, using a starting material which had not previously been used for that process. The process itself was

known. The court held that the process was obvious, but it cautioned against using its decision as precedent in other situations:

> We reiterate another principle followed in obviousness issue cases, which is to decide each case on the basis of its own particular fact situation. What we or our predecessors may have said in discussing different fact situations is not to be taken as having universal application.

The present case involves, in the case of claims 13-17, various forms of apparatus for dispensing azelastine into nasal or eye tissues. This is a different fact situation from the Durden case. For the reason given in the quoted passage, we submit that Durden does not deal with the patentability of this type of claim.

Furthermore, in Durden, the Court distinguished the fact situation from that in In re Kuehl, 475 F.2d 658 (C.C.P.A. 1973) where the result of the process was not foreseeable. In the present case, where there is evidence of a surprising result, it is submitted that the holding of Durden is not applicable, for the same reason as that which distinguished Durden from Kuehl.

The Kuehl case is much more relevant to the present case than Durden. The question in Kuehl was whether it was obvious to use a new zeolite in a catalytic process which had been used previously with other zeolites. The Court held that prior cases, relating to the obviousness of using a known process of making a new substance, were not relevant to that question. Further, the Court held that it was appropriate to consider the surprising result which was achieved with the new zeolite:

> We note that in the present case the novel catalyst, ZK-22, is not merely itself reduced but itself catalyzes the

hydrocarbon charge in the claimed process, a result that was not predictable until appellant had made his invention.

In the present case, the claimed articles produce a result which was not foreseeable from the teachings of the prior art, and, therefore, it is submitted that the articles of claims 13-17 are patentable.

Favorable reconsideration and allowance are respectfully requested.

The applicants have informed us that the following documents have been cited in counterparts of the present application:

German Application:

Published German Patent Application DE-OS 21 64 058, corresponding to U.S. Patent 3,813,384

Arzneimittel, Fortschritte 1972-1985, Pages 936 and 939 (1977)

Org.-Chem. drugs and their symptoms, Vol. III,m No. 6496 (1987)

European Application:

German Patent Application 3 530 793, corresponding to U.S. Patent 4,704,387.

Copies of these documents are attached.

Respectfully submitted,

CUSHMAN, DARBY & CUSHMAN

By Lawrence A. Hymo

Lawrence A. Hymo

Reg. No. 19,057